MASARYKOVA UNIVERZITA

Attachment No. 12:

Public lecture evaluation

Masaryk University	
Faculty	Faculty of Science
Field of study	Biomolecular Chemistry
Applicant	***Mary O'Connell, Ph.D., MS***
Unit	Head – ERA Chair - Mary O'Connell Research Group
Lecture date	26 09 2017
Lecture topic	**The biological role of inosine in RNA**
Persons present	(see attendance sheet – attached to evaluation report)
Designated evaluators	Prof. RNDr. Julius Lukeš, CSç. *Faculty of Science, University of South Bohemia, České Budějovice*
(board members)	Prof. RNDr. Ivan Raška, DrSc. *First Faculty of Medicine, Charles University, Prague*
	Prof. Mag. Dr. Renée Schröder *Max F. Perutz Laboratories, Vienna*
	Prof. RNDr. Tachezy, Ph.D. *Faculty of Science, Charles University, Prague*
	Prof. RNDr. Vladimír Sklenář, DrSc. *CEITEC Masaryk University, Brno*

Reviewer's report

The ADAR enzymes convert adenosine to inosine in dsRNA. In the seminar, Mary O'Connell has started with a historical perspective and described the initial discovery of the ADAR enzymes, their purification and the subsequent cloning of both enzymes. Next part covered biochemical characterization of both enzymes, their localization with the cell, their function as dimers, post-translational modifications of the proteins and how this impacted on their biological function.

A genetic approach undertaken by her group was reported and both mice and *Drosophila* used as model organisms described. *Drosophila* were generated transgenically that had no ADAR protein. These flies were barely viable and had problems walking and were sterile. As the flies aged they accumulated holes in their brain. Subsequent work by her group has recently shown that these holes are due to the cells inability to degrade proteins and large cellular complexes. *Drosophila* have proven to be an excellent system for studying ADAR activity as genetic screens for regulators of ADAR function can be performed in this organism. These genetic screens have been undertaken and have uncovered some interesting

factors that ADAR interacts with, such as ecdysone signalling pathway which is one of the major pathways involved in *Drosophila* development.

It had been shown by other groups that *Adar1* mice died while they were embryos and for 10 years different groups investigated this and tried to determine what caused this lethality. The O'Connell group were the first to rescue the mutant mice so that they were born alive and showed that the ADAR1 protein is essential in mammals for the innate immune response. Basically the protein is responsible for the occurrence of inosine in RNA which is not found either in bacterial or viral RNA. Thus, when the cell encounters RNA containing inosine it recognises that it is 'self' and does not generate an immune response against it. In collaboration with the group of Yanick Crow they demonstrated that mutation in *ADAR1* causes Aicardi-Goutieres Syndrome, a fatal childhood disease, in which the children mount an immune response to their own RNA.

Conclusion

The lecture delivered by Mary O'Connell, entitled **"The biological role of inosine in RNA"** and delivered as part of her professorship procedure, ***demonstrated*** sufficient scholarly qualifications and pedagogical capabilities expected of applicants participating in a professor appointment procedure in the field of Biomolecular Chemistry.

Brno, September 26, 2017

Prof. RNDr. Julius Lukeš, CSc

Prof. RNDr. Ivan Raška, DrSc.

Prof. Mag. Dr. Renée Schröder

Prof. RNDr. Jan Tachezy, Ph.D.

Prof. RNDr. Vladimír Sklenář, DrSc